

In re Application of: Eshel BEN-JACOB et al.  
Serial No.: 10/534,127  
Filed: November 18, 2005  
Office Action Mailing Date: December 3, 2008

Examiner: Lee S. COHEN  
Group Art Unit: 3739  
Attorney Docket: 29752

**In the Claims:**

1-368. (Canceled)

369. (Currently Amended) A device for positioning at least one cell in at least one addressable position, the device comprising a non-conductive substrate formed with:

(a) at least one addressable pore; and

(b) at least one channel embedded in said substrate and being in fluid communication with said at least one pore; and

(c) at least one electrode structure positioned in said at least one pore and protruding from a surface of said substrate;

said at least one pore and said at least one channel being designed and constructed such that an under-pressure formed in said at least one channel results in vacuum adherence of the at least one cell onto said at least one pore, such that a single cell is vacuum adhered onto a single pore.

370. (Previously Presented) The device of claim 369, further comprising a plurality of addressable pores and a plurality of channels and being suitable for positioning a plurality of cells in a plurality of addressable positions.

371. (Previously Presented) The device of claim 369, wherein said substrate is coated with a coat or having a chemically modified surface, so as to enhance affinity adherence of cells thereto and growth of cells thereon.

372. (Previously Presented) The device of claim 371, wherein said coat or chemically modified surface is patterned.

373. (Previously Presented) The device of claim 372, wherein said coat or chemically modified surface is discontinuous.

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374. (Previously Presented) The device of claim 373, wherein said coat or chemically modified surface is restricted to areas on said substrate surrounding said at least one pore.

375. (Currently Amended) The device of claim 369, wherein said substrate is attachable to ~~designed and constructed locatable on an organ.~~

376. (Currently Amended) The device of claim ~~375~~369, wherein said organ is ~~designed and constructed locatable on a brain.~~

377. (Currently Amended) The device of claim 369, wherein at least said substrate is ~~designed and constructed implantable in an animal.~~

378. (Previously Presented) The device of claim 375, wherein said substrate is flexible.

379. (Canceled)

380. (Currently Amended) The device of claim 370, wherein said substrate is ~~a non-conductive substrate and is further~~ formed with a plurality of electrode structures, each being positioned in one of said plurality of addressable pores.

381. (Currently Amended) The device of claim ~~369~~379, wherein said electrode structure is emerging from a base of said at least one pore ~~and protrudes from a surface of said substrate.~~

382. (Currently Amended) The device of claim 380, wherein ~~each~~ at least one of said plurality of electrode structures is emerging from a base of one of said plurality of addressable pores and is flush with a surface of said substrate.

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383. (Previously Presented) The device of claim 380, wherein each of said electrode structures is designed and constructed to penetrate into a cell adhered thereto.

384. (Canceled)

385. (Previously Presented) The device of claim 380, wherein each of said electrode structures is substantially perpendicular to said substrate.

386. (Currently Amended) The device of claim 369379, designed and constructed such that when a cell adheres to said electrode structure, leakage of intracellular components of said cell is prevented.

387. (Currently Amended) The device of claim 369379, wherein said at least one electrode structure has hydrophobic properties.

388. (Previously Presented) The device of claim 369, wherein said at least one channel and said at least one pore are designed and constructed so as to allow administration therethrough of at least one substance to the at least one cell.

389. (Previously Presented) The device of claim 370, wherein said plurality of channels and said plurality of addressable pores are designed and constructed so as to allow administration therethrough of different substances to different cells of said plurality of cells.

390. (Currently Amended) The device of claim 369379, wherein said substrate is further formed with at least one conductive element embedded therein and electrically coupled to said at least one electrode structure.

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391. (Previously Presented) The device of claim 380, wherein said substrate is further formed with a plurality of conductive elements embedded therein and electrically coupled to said plurality of electrode structures.

392. (Previously Presented) The device of claim 391, wherein said plurality of conductive elements and plurality of channels are devoid of electrical coupling thereamongst.

393. (Previously Presented) The device of claim 392, wherein said plurality of conductive elements and said plurality of channels are formed at different layers within said non-conductive substrate.

394. (Previously Presented) The device of claim 391, further comprising a coded interface electrically coupled with said plurality of conductive elements and being connectable to a system of amplifiers.

395. (Previously Presented) The device of claim 391, further comprising a system of amplifiers integrally formed on or in said substrate and being electrically coupled with said plurality of conductive elements.

396. (Previously Presented) The device of claim 394, wherein said coded interface comprises a plurality of transmission lines, each transmission line being electrically coupled to one of said plurality of conductive elements.

397. (Currently Amended) The device of claim ~~369379~~, wherein a voltage sensitivity of said at least one electrode is selected so as to allow sensing intracellular potentials.

398. (Canceled)

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399. (Currently Amended) The device of claim ~~369~~379, wherein a voltage sensitivity of said at least one electrode is selected so as to allow transmitting stimuli to the at least one cell.

400. (Previously Presented) The device of claim 370, further comprising a pump being in fluid communication with said plurality of channels, said pump and said plurality of channels being designed and constructed so as to provide an equally distributed pressure drop over said plurality of addressable pores.

401. (Withdrawn-Currently Amended) A system for measuring electrical activity of a plurality of cells, the system comprising:

(a) ~~A~~a non-conductive substrate formed with a plurality of addressable pores and a plurality of channels embedded in said substrate and being in fluid communication with said plurality of addressable pores;

(b) ~~A~~a plurality of multi-electrode-arrays, each one of said plurality of multi-electrode-arrays includes a plurality of electrode structures formed on a first side of said non-conductive substrate and positioned in one of said pores such that at least one of said electrode structures protrudes from a surface of said first side; and

(c) a plurality of conductive elements formed on a second side of said non-conductive substrate, wherein each one of said conductive elements is electrically coupled to one of said electrode structures; and

(ed) ~~A~~a fluid source being in fluid communication with said plurality of channels;

said pores, said channels, said electrode structures and said fluid source are designed and constructed so that said electrode structures sense electrical signals from the plurality of cells while said fluid source continuously exchanges fluids with said channels and pores.

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402. (Withdrawn) The system of claim 401, wherein said pores and said channels are designed and constructed such that an under-pressure formed in said channels results in vacuum adherence of the plurality of cells onto said plurality of addressable pores, such that a single cell of the plurality of cells is adhered onto a single pore of said plurality of addressable pores.

403. (Withdrawn) The system of claim 402, further comprising a pump being in fluid communication with said plurality of channels, said pump and each of said plurality of channels being designed and constructed so as to provide an equally distributed pressure drop over said plurality of addressable pores.

404. (Withdrawn) The system of claim 401, further comprising a system of amplifiers being electrically coupled with said plurality of conductive elements.

405. (Withdrawn) The system of claim 401, wherein said system of amplifiers are integrally formed on or in said non-conductive substrate.

406. (Withdrawn) The system of claim 404, further comprising at least one data processor, electrically coupled to said system of amplifiers via at least one acquisition board, for acquiring and processing data collected from said plurality of electrode structures.

407. (Withdrawn) The system of claim 406, further comprising at least one multiplexer, being in electrical communication with said at least one data processor, wherein each one of said at least one multiplexer combines at least two communication channels originated from said acquisition board.

408. (Withdrawn) The system of claim 406, further comprising a stimulator electrically communicating with said at least one data processor, for generating

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temporal stimulating electrical signals, transmitted via said electrode structures to the cells at predetermined intervals and in predetermined durations.

409. (Withdrawn) The system of claim 408, wherein said stimulator is designed and configured so as prevent electrolysis process within said electrode structures.

410. (Currently Amended) A method of positioning at least one cell in at least one addressable position, the method comprising:

providing a substrate formed with at least one addressable pore, ~~and~~ at least one channel embedded in said substrate and being in fluid communication with said at least one pore, and at least one electrode structure positioned in said at least one pore and protruding from a surface of said substrate;

spreading a liquid medium and said at least one cell over said substrate;  
and

generating an under-pressure in said at least one channel so as to adhere the at least one cell onto said at least one pore via vacuum adherence, such that a single cell vacuum adhered onto a single pore, thereby positioning the at least one cell in the at least one addressable position.

411. (Previously Presented) The method of claim 410, wherein the at least one cell is electrically excitable.

412. (Previously Presented) The method of claim 410, wherein the at least one cell is selected from the group consisting of a neuron cell, a heart cell, a muscle cell and a pancreatic cell.

413. (Previously Presented) The method of claim 410, further comprising sensing electrical signals of the at least one cell via at least one electrode structure.

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414. (Previously Presented) The method of claim 413, wherein said sensing is by penetrating the cells, using said at least one electrode structure.

415. (Canceled)

416. (Previously Presented) The method of claim 410, further comprising administering at least one substance to said at least one cell via said at least one channel and said at least one addressable pore.

417. (Previously Presented) The method of claim 410, further comprising continuously exchanging fluids between a fluid source and said at least one channel and at least one pore.

418. (Withdrawn-Currently Amended) A method of measuring electrical activity of a plurality of cells, the method comprising:

(a) providing a non-conductive substrate formed with a plurality of addressable pores and a plurality of channels embedded therein and being in fluid communication with said plurality of addressable pores;

(b) spreading a liquid medium and said cells over said substrate;

(c) sensing electrical signals of the cells via a plurality of multi-electrode-arrays, wherein each one of said plurality of multi-electrode-arrays includes a plurality of electrode structures formed on a first side of said non-conductive substrate and positioned in one of said pores such that at least one of said electrode structures protrudes from a surface of said first side; and

(~~gd~~) continuously exchanging fluids between a fluid source and said channels and pores ~~a fluid source being in fluid communication with said plurality of channels;~~

thereby measuring the electrical activity of the plurality of cells.



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419. (Withdrawn) The method of claim 418, wherein said sensing electrical signals and said continuously exchanging fluids is executed substantially contemporaneously.

420. (Withdrawn) The method of claim 418, wherein the plurality of cells are electrically excitable.

421. (Withdrawn) The method of claim 418, wherein the plurality of cells are selected from the group consisting of a neuron cell, a heart cell, a muscle cell and a pancreatic cell.

422. (Withdrawn) The method of claim 418, further comprising generating an under-pressure in said channels so as to adhere the plurality of cells onto said plurality of addressable pores via vacuum adherence, such that a single cell of the plurality of cells is adhered onto a single pore of said plurality of addressable pores.

423. (Withdrawn) The method of claim 422, wherein said generating said under-pressure is done so as to provide an equally distributed pressure drop over said plurality of addressable pores.

424. (Withdrawn) The method of claim 418, wherein said sensing is by penetrating the cells, using said electrode structures.

425. (Withdrawn) The method of claim 418, wherein said sensing is by externally engaging the cells using said electrode structures.

426. (Withdrawn) The method of claim 418, further comprising administering at least one substance to said cells via said channels and said pores.

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427. (Withdrawn) The method of claim 418, further comprising acquiring and processing data collected from said plurality of electrode structures using at least one data processor.

428. (Withdrawn) The method of claim 418, further comprising generating temporal stimulating electrical signals, and transmitting said stimulating electrical signals via said electrode structures to the cells at predetermined intervals and in predetermined durations.

429. (Withdrawn) The method of claim 428, wherein said stimulating is done so as prevent electrolysis process within said electrode structures.

430. (New) A device for positioning at least one cell in at least one addressable position, the device comprising a non-conductive substrate formed with:

- (a) at least one addressable pore;
- (b) at least one channel embedded in said substrate and being in fluid communication with said at least one pore; and
- (c) at least one electrode structure emerging from a base of said at least one pore;

said at least one pore and said at least one channel being designed and constructed such that an under-pressure formed in said at least one channel results in vacuum adherence of the at least one cell onto said at least one pore.